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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

An approach for imaging electric tissue properties in vivo is proposed. The technique relies upon the integration of MRI data with electrical potential measurements made over the surface of the patient. Through a technique referred to as constrained electric impedance tomography, the conductivity of specific regions identified in MRI data can be calculated. This work is a numerical simulation of the physics and mathematics of this concept.
A two-dimensional simulation of a simple structure containing three-regions of varying electrical conductivity was generated and a finite-element model of electrical current propagation created. By arranging 24 electrodes around the object and numerically applying a voltage between a pair of them, the voltages between other pairs of electrodes were calculated using the finite-element model. This was repeated by numerically applying a voltage between other electrode pairs. These simulated voltage data were then used in conjunction with the known spatial distribution of object components to solve for their unknown electrical conductivity. An iterative nonlinear optimization technique was used to find the electrical conductivity distribution that minimizes the difference between the calculated voltages and the simulated input data. In the absence of noise, the reconstruction was excellent; however, it was shown to degrade in the presence of experimental noise. Nevertheless, the stability of the reconstruction suggested that the technique will be practical in an experimental system. We will continue these stimulations during the course of next year.

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INTRODUCTION

Magnetic resonance imaging (MRI) has become an invaluable tool in the detection and diagnosis of disease. During the past several years, we have been exploring the role of MRI in the detection of breast cancer and in particular its role in the screening of women at elevated risk arising from mutations to the breast cancer genes BRCA1/BRCA2. Our studies have shown that breast MRI offers significant advantage over other breast imaging modalities for the detection of breast cancer in younger women, who present with dense breasts and for whom breast cancer prognosis is often poor. In the course of our work, we have shown that the sensitivity of breast MRI is high (> 90%) which is consistent with findings from a number of other centers who have studies of breast MRI in the general diagnostic population[i]. This is particularly important as MRI exhibits high sensitivity in this special, high-risk group, in whom high breast density is frequently present; a feature which often limits imaging by mammography. This work, together with finding from other studies, suggests that MRI will play a critical role in breast imaging in the future.

While the sensitivity of breast MRI is high, the specificity remains less than ideal. As some kinds of normal tissue (lymph nodes), benign processes (fibroadenomas) as well as malignant tumours can show signal increases under Gd-DTPA enhanced MRI, the clear distinction of these different tissue types is challenging. Various approaches to address this problem are based on the use of kinetics of assessment and lesion morphology. Several studies have shown that specificity can vary significantly depending on the patient population and the approach used. Drawn from the work of a number of investigators, the specificity of MRI has been reported with values ranging from 37%-97% [ii]. Probably of greater interest, is the positive predictive value (PPV), that reflects the frequency with which MRI detected lesions sent to biopsy prove to be malignant. In our own experience, we found a PPV of 26% from data drawn from our first year of screening. During subsequent years, our PPV increased substantially; however, the issue of improving the PPV remains an important research objective. This motivates us to explore other areas whereby the specificity and PPV of breast MRI can be improved.

ELECTRIC IMPEDANCE TOMOGRAPHY (EIT)

A number of investigators have proposed the use of electric fields to probe tissues deep within the body. As electrical current moves through a tissue, it propagates in a way depending on its electrical impedance. Previous investigations have shown that electric impedance changes widely among varying tissues, with cancer generally exhibiting lower impedance than corresponding normal and benign tissues[iii]. This finding has motivated a great deal of interest in this electric impedance measurement as an imaging modality referred to as electric impedance tomography (EIT). In operation, EIT derives its data from an array of electrodes that surround the body which are used to inject, current into the body at various points which generate surface potentials measured at all points surrounding the body. In a manner similar to computer tomography, images of the electrical properties of tissue are then computed[iv] from these measurements.

While this area is an active area of research pursuit, stable and robust inversion techniques for electrical impedance images are lacking. The cause is fundamental and arises from the fact that changes in electrical measurements made at the skin surface change in a very subtle manner with variations of tissue impedance deep within the body. As such, the spatial resolution offered by EIT is limited. Furthermore, the presence of noise in the measured data can have large consequence on the stability of the reconstructed data. As a result of these two features, the inverse problem associated with EIT image reconstruction is considered to be ill posed. This factor represents a major barrier to progress in this field and its subsequent introduction into clinical practice.

CONSTRAINED ELECTRICAL IMPEDANCE TOMOGRAPHY (CEIT)

Given the unique possibility to probe tissues in a new and non-invasive manner, the goal of achieving EIT for breast imaging is indeed enticing. However, the issue of resolution and the ill-posed nature of the inverse problem remains a fundamental issue. In this work, we propose an alternative approach in which we believe the inverse problem associated with EIT can be substantially simplified and may create a new direction for this field.

As our interest is in breast MRI, the task of detecting relevant lesions is well handled by the use of Gd-DTPA enhancement as outlined above. Furthermore, breast MRI provides three-dimensional information about the distribution of normal tissue and the size and location of the suspected tumour within the breast. As such, we propose to combine these two imaging approaches to use this additional information to constrain the reconstruction of the EIT data with a-priori MRI

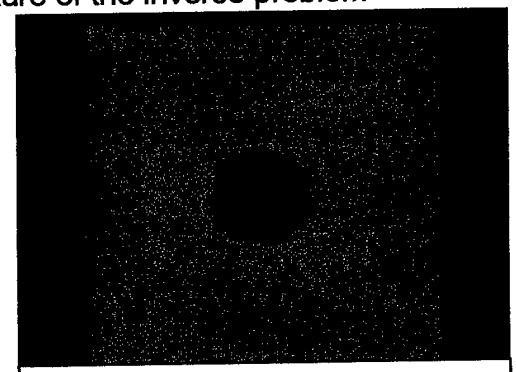

Figure 1. A three-compartment model to study the CEIT problem. The relative conductivity of the three regions (green:orange:red) were set at 1:5:25 units. A total of 24 electrodes were placed around the object as shown by tiny points on the object periphery.

information. As such, we refer to this modification of EIT as Constrained Electrical Impedance Tomography (CEIT).

The concepts of constrained reconstruction for breast imaging has been largely motivated by other work we have conducted in the area of Elastography[v]. In this application, we consider a different inverse problem, in which mechanical motion throughout tissue can be used to report tissue biomechanical properties. To solve this problem, we have developed a constrained reconstruction approach in conjunction with phase contrast MRI to measure tissue Young's modulus. Our goal in this study is to apply this class of solution to the CEIT problem.

RESEARCH TASKS

This project was aimed at providing basic theoretical evidence that CEIT would be practical and of advantage over EIT. Specifically, we proposed to develop an appropriate approach for CEIT and explore its application in numerical simulations. Our goal was to determine the noise properties of the system and its potential accuracy in simple phantom geometries.

PROGRESS TO DATE:

The study involves creating a model problem with an appropriate distribution of electrodes and voltage measurements. Figure 1 shows our model problem as three regions with conductivities of 1, 5 and 25 S/m. A total of 24 electrodes are distributed around the object (seen as tiny black marks on the periphery of the object). A mesh for the model is then created for finite element modeling. The relation between the potential and electric current is modeled in the form of a variational integral boundary value problem in the following as:

$$\int_V \nabla \delta\Phi \cdot \sigma \cdot \nabla \Phi dV = \int_S \delta\Phi J dS$$

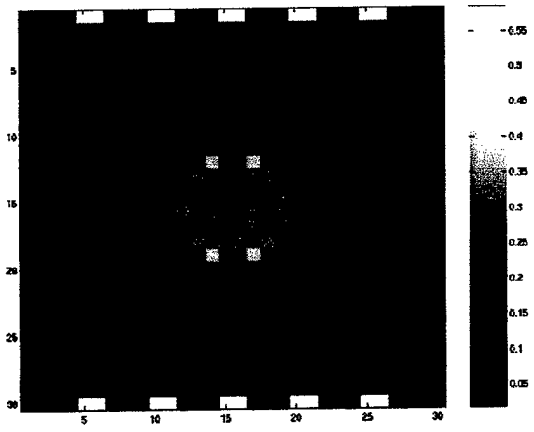

Figure 2.Calculated current for the phantom with a uniform potential across the top array of electrodes.

where Φ is the electrical field potential, σ is the tissue conductivity, and J is the current density [vi]. The surface potential is calculated for a given set of boundary conditions by finite element methods. A typical current distribution for a calculation when the potential is uniform across the top of the phantom is shown in Figure 2. Here we can see the central inclusion clearly as a region of higher current density passing through this region compared to the surrounding regions of lower conductivity.

CONSTRAINED RECONSTRUCTION

The essence of the constrained reconstruction is to create a model of the object for forward calculations of the electric fields and compare results derived from this model field to those derived experimentally. For example, the current injection and the potential measurements could be made as shown in Figure 3. Given that there is a number of potential current injection, grounding and measurement points, a large number of measurements can be made. To solve for the unknown conductivities, we use an non-linear optimization algorithm to estimate the conductivities in a series of steps, whereby the values for the three regions are adjusted iteratively until the difference between the predicted potentials and those seen experimentally is minimized. This algorithm makes the assumptions that the conductivity is isotropic and uniform within a specified region. In this case, three unknown values of conductivity are to be determined, while the spatial extent of these regions is to be inferred from the MRI data. The question that remains is the stability of the estimation, its accuracy and the sensitivity to noise in the measurement data itself.

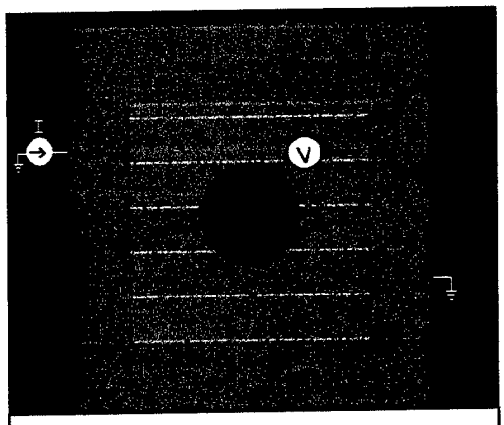

Figure 3. A potential measurement across a pair of electrodes for a given geometry of applied voltage.

RESULTS

Based on this simple geometry we have found that it is possible to reconstruct the values of the three regions with high accuracy in the absence of measurement noise. The reconstructions are stable and converge rapidly. However, in the presence of measurment noise, we begin to see the effects on the final values for each region. In our study, we calculated the effect of adding noise to the measurement values that were 1%, 5% and 10% of the potential at the voltage injection site throughout all the measurement points. This data is shown in Table I. The ideal ratio of conductivities should be 1:5:25. With small noise levels, it is clear that the accuracy is good but it begins to degrade with increased noise levels approaching 10%. The noise value, as applied, represents a measure of the noise level introduced on each measurement as a fraction of the applied potential. While a useful first approximation of noise, this tends to overestimate the relevant noise in the detected signals. These simulations indicate that reconstructions can indeed be performed in a stable manner as seen by the limited number of interactions needed to reach a convergent value. The system is robust in the presence of noise and clearly warrants further analysis.

Table 1. Estimated conductivity for the three regions (C1, C2, and C3), the residual of the optimization problem and number of iterations required for convergence as a function of source noise levels. The ideal ratio of C1:C2:C3 is 1:5:25.

Noise	Residual	C1 (S/m)	C2 (S/m)	C3 (S/m)	Ratio	Iteration #
1%	1.23	0.99	5.0	24.48	1:5.1:24.7	8
5%	34.8	0.82	4.02	24.33	1:4.9:30	20
10%	140.6	0.56	6.75	20.81	1:12.2:37.5	15

FUTURE WORK

During the coming months, we will be continuing to explore this problem with numerical simulations. We will continue to optimize our inverse solution approach and study the noise characteristics in a way that is more realistic experimentally. Our current simulations have been done in 2 dimensions for the purposes of computational efficiency. We will explore the extension to 3D in the coming months. Finally, we will use 3D breast MRI data as a test bed, in which more complex meshes that reflect the way real tissue could occur. This will set the stage for considering the effects of varying the number and pattern of electrodes over the imaging volume and the corresponding impact on reconstruction accuracy and stability. Our overall goal is to determine whether this concept is practical for application in conjunction with our existing breast MRI techniques. If this work proves to be reasonable, we propose to explore it experimentally in a future proposal, under a different funding mechanism. To conduct this work over the next year, we have requested and received a no cost budget extension.

KEY RESEARCH ACCOMPLISHMENTS:

We have devised a novel method for conducting measurement of electrical conductivity within specified regions of tissues derived form medical imaging data. The specific accomplishments to date are:

1) The development of a 2D finite element model of electric fields and currents in arbitrary structures,

2) Software development of the constrained reconstruction process for electrical impedance measurements

3) Exploration of a number of iteration details to provide maximum stability

4) Study of the accuracy and stability of the reconstruction process under different noise levels.

5) We have demonstrated that CEIT offers significant advantages over EIT in our application and as such is worthy of further research.

CONCLUSIONS

We are excited about the results that we have found at this point of our study and are encouraged to continue with this line of investigation. The potential for integrating CEIT with MRI breast imaging represents a unique and novel approach, which to the best of our knowledge, has not been proposed before. The potential to elucidate new information that will aid in the appreciation of masses detected in contrast enhanced breast MRI is significant. This represents an example of how constrained integration of 3D imaging data with other imaging or biological probes can be used. It represents a general approach that will allow the integration of a wider array of potentially interesting biological signals, of which electrical conductivity is but one example.

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